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Introduction

Robot-assisted laparoscopic radical prostatectomy (RALP) has been used worldwide in the treatment of localized prostate cancer because of its minimal invasiveness compared to open retropubic radical prostatectomy (RRP) (1,2). RALP provides a number of benefits, such as reduced blood loss, less postoperative pain, and shorter hospital stay than other methods. However, RALP requires a steep Trendelenburg (head-down) position and CO₂ pneumoperitoneum for several hours to secure the surgical visual field. The steep Trendelenburg position and pneumoperitoneum cause significant changes in cardiovascular, respiratory, and neurophysiological parameters (3,4). Pneumoperitoneum influences intrathoracic pressure by pushing the diaphragm upward, and the head-down position further changes the position of the intestine and diaphragm, thus reducing lung volume and decreasing respiratory system compliance. Pneumoperitoneum with head-down position also causes circulatory perturbation. The

mean arterial pressure (MAP) as well as right and left ventricular filling pressures, e.g., central venous pressure and pulmonary capillary wedge pressure, increase markedly under these conditions (5).

There have been several reports of anesthetic complications after RALP—a patient with post-extubation respiratory distress required reintubation and subsequent ventilation in an intensive care unit (6), a patient developed sudden pulmonary edema after uneventful RALP (7), and two patients developed postoperative ischemic optic neuropathy after RALP(8). These complications were mainly caused by steep head-down position and pneumoperitoneum during the operation.

Some previous studies indicated the influence of head-down position and pneumoperitoneum on the cardiovascular and respiratory system during RALP. However, to our knowledge, the effects of different head-down angles on cardiac and respiratory function have not been determined during RALP. The present study was performed to investigate the influence of different Trendelenburg position angles with pneumoperitoneum during RALP on cardiovascular and respiratory homeostasis.

Materials and methods

Approval for the study was obtained from Institutional Ethics Committee at

Kanazawa University Hospital. After obtaining written informed consent, 48 patients, who were assessed with the American Society of Anesthesiologists Physical Status (ASA PS) classification system and evaluated as ASA PS 1 or 2, were recruited. Patients with a history of valvular heart disease, myocardial infarction, chronic obstructive or restrictive pulmonary disease, heavy smoking, renal insufficiency, or neurological disease were excluded from the study. Each patient selected RRP or RALP, and 12 patients undergoing RRP and 36 patients undergoing RALP were enrolled in this study. The patients who selected RALP were randomly divided into three groups: each patient placed in the 20°, 25°, or 30° head-down position during the operation (Fig.1). But there was a concern of the sight of the operation space with a patient selected in the 20° head-down position after checking through the intra-abdominal camera, therefore the patient underwent RALP with 30° head-down position and excluded from this study. Finally, 11 patients undergoing RALP in the 20° head-down position, 12 patients in the 25° and 12 patients in the 30° were enrolled in this study.

No premedication was administered. After applying routine monitors and establishing intravenous access, anesthesia was induced intravenously with propofol (1.0 – 2.0 mg/kg) and remifentanyl (0.5 mg/kg/min). Muscle paralysis was produced by rocuronium (0.6 mg/kg) and the trachea was intubated. General anesthesia was

maintained with sevoflurane in oxygen and remifentanyl (0.1 – 0.3 mg/kg/min). The fraction of inspired oxygen was varied from 0.33 to 0.5 to maintain peripheral oxygen saturation over 98%. Rocuronium administration was repeated as needed for muscle relaxation. After induction of general anesthesia, a 22-gauge arterial cannula was inserted for continuous arterial pressure monitoring and blood sampling. Ventilation was performed with breathing gas 40% oxygen in air, inspiratory fresh gas flow of 3.0 L/min, and inspiration: expiration ratio of 1:2. Tidal volume was set at 10 mL/kg initially. The ventilation mode was controlled by mechanical ventilation without positive end-expiratory pressure (PEEP) at the beginning of the operation, but after the abdominal cavity was insufflated with CO₂ gas pressure set to 12 mmHg and the patient was placed in the Trendelenburg position, the mechanical ventilation was adjusted to maintain end-tidal CO₂ concentration at 30 to 40 mmHg. The pressure of pneumoperitoneum was maintained at 12 mmHg during the laparoscopic procedure.

RALP was performed with the da Vinci Surgical System (Intuitive Surgical Inc., Sunnyvale, CA) via the transperitoneal approach. After insufflation of the abdominal cavity with CO₂ to a pressure of 12 mmHg, six abdominal ports were placed with the patient in the horizontal position. The patient was then placed in the Trendelenburg position. RALP was performed using the transperitoneal approach. At the end of the

procedure, pneumoperitoneum was released and the patient was returned to the horizontal position. RRP was performed using the extraperitoneal retropubic approach in the spine position. A single surgeon operated on all RALP cases with same procedure.

Heart rate (HR), mean arterial pressure (MAP), respiratory rate (RR), end-tidal CO₂ pressure (PetCO₂), tidal volume (Vt), and peak inspiratory pressure (PIP) were recorded immediately after induction of anesthesia (T0; baseline), 5 min after induction of pneumoperitoneum in the supine position in RALP (T1); 5, 15, 30, and 120 min after placement in the Trendelenburg position with pneumoperitoneum in PALP; and 5, 15, 30, and 120 min after starting the operation in open prostatectomy (T2, T3, T4, and T5); 5 min after desufflation in the supine position in RALP (T6); and at skin closure in the supine position (T7). Dynamic compliance (C_{dyn}) was calculated with the following equation: $C_{dyn} = Vt / (PIP - PEEP)$.

Statistical analyses were performed using the R statistical package (version 2.11.1; R Foundation for Statistical Computing). Means and standard deviations of each group were calculated. Differences in mean values of the data of each group were tested by one-way analysis of variance (ANOVA) for normally distributed data or Kruskal–Wallis test for non-normally distributed data with Games–Howell post hoc tests assuming non-equal variances between the groups. Simple linear regression analysis was

performed to examine relationships between MAP, PIP, Cdyn, and angle of head-down tilt, and the correlation coefficients were calculated. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

There were no significant differences in patient characteristics or operative data between the four groups, with the exception of blood loss (Table 1)—RRP was associated with significantly greater blood loss than RALP. Hemodynamic and respiratory data are listed in Table 2. The RRP group did not show any significant changes in the variables monitored throughout the study. HR was maintained constant during the study period and did not differ significantly between the groups. MAP was increased significantly with pneumoperitoneum at T1, and showed a much greater increase in the first 5 min after placing in the Trendelenburg position. After that, the MAP decreased modestly and did not increase significantly after T4 in the RALP 20° group or after T5 in the RALP 25° and 30° groups. RR increased significantly at T2, T3, T4, and T5 in the RALP groups and decreased after desufflation in the supine position. PetCO₂ increased gradually after establishment of pneumoperitoneum, increased significantly after additional Trendelenburg position and decreased gradually after

desufflation in the supine position. PIP rose significantly with pneumoperitoneum in all PALP groups, and a further significant increase in PIP was observed with the additional Trendelenburg position in the RALP 25° and 30° groups compared with pneumoperitoneum only. After deflation, PIP returned immediately to a level not significantly higher than that at T0. Cdyn decreased significantly with pneumoperitoneum at T1 and further decreased with additional Trendelenburg position although this was not significant. Cdyn returned to the control level after deflation. Among 3 different RALP groups, only Cdyn showed a significant difference with the angle of head-down tilt between 20° and 30° at T2.

There were significant correlations between the angle of head-down tilt and MAP at T2 ($R = 0.46$, $P = 0.005$), T3 ($R = 0.39$, $P = 0.021$), T4 ($R = 0.37$, $P = 0.012$) and T4 ($R = 0.38$, $P = 0.026$) (Fig.2A), PIP at T3 ($R = 0.41$, $P = 0.014$), T4 ($R = 0.45$, $P = 0.006$) and T5 ($R = 0.34$, $P = 0.042$) (Fig.2B), and Cdyn at T2 ($R = 0.52$, $P = 0.002$), T4 ($R = 0.34$, $P = 0.048$), and T5 ($R = 0.37$, $P = 0.027$) (Fig.2C). There were no significant correlations between the head-down setting and HR, RR, or PetCO₂. MAP decreased gradually over time in each group during the Trendelenburg position with pneumoperitoneum. As the angle of head-down tilt increased, MAP, RR, PetCO₂, and PIP tended to increase and Cdyn tended to decrease. The patients enrolled in this study

tolerated the anesthesia and the procedure without complications.

Discussion

The results of this study demonstrated that the degree of head-down angle of RALP affected the cardiovascular and respiratory parameters. In comparison with open prostatectomy, significant differences were observed in the measured parameters other than HR associated with pneumoperitoneum and the head-down position. Cdyn at T2 showed significant differences between 20° and 30°. The cardiovascular and respiratory values tended to worsen with greater head-down angle. Only 20°, 25°, and 30° were examined in this study; however, much deeper head-down positions are expected to have stronger effects on the cardiovascular and respiratory system of the patient.

Previous reports have indicated both increased HR and no change associated with pneumoperitoneum with head-down position (3,9). In the present study, we found no significant changes in HR. MAP increased significantly with pneumoperitoneum as reported previously (4,5,10), and showed greater increases by up to 20% with 20° head-down position and increased to 31% with 30° head-down position compared with baseline. The MAP change is due to increased intraabdominal pressure by pneumoperitoneum compressing the aorta and increasing afterload, and hormonal

effects, such as catecholamine and vasopressin, secreted by peritoneal stretching and sympathetic stimulation due to hypercapnia (11,12). However, the hormonal effects of pneumoperitoneum with head-down position have not been clarified (13).

Lung compliance is significantly reduced by pneumoperitoneum, and greater decreases were observed up to 41% and 51% with 20° and 30° head-down position, respectively. The thoracic cavity was compressed by the increase in abdominal pressure and diaphragmatic elevation by pneumoperitoneum, and it was suggested that elevated thoracic pressure was promoted by the head-down position (4,5,10). The present study indicated that deeper head-down position caused a greater decrease in lung compliance. A mechanism similar to lung compliance is thought to be responsible for the observations related to PIP.

Other studies have indicated similar significant PetCO₂ changes due to pneumoperitoneum with head-down position (4,5,10). The anesthesiologist adjusted the number of breaths with a rise of PetCO₂, and RR increased similar to PetCO₂. PetCO₂ is acceptable as a reliable means of assessing arterial CO₂ (PaCO₂) during short-lasting laparoscopic surgery (14,15). The relation between PetCO₂ and PaCO₂ is unreliable after increased laparoscopic operating time. The inconstant correlation between PetCO₂ and arterial PaCO₂ was reported to be due to several possible reasons, such as inter- and

intraindividual variability, duration of Trendelenburg position, and pneumoperitoneum (16). Arterial blood sampling for CO₂ measurement is recommended at any time point during RALP, and the anesthesiologists at our institution sometimes check PaCO₂ during the operation.

Relatively high pneumoperitoneum with steep Trendelenburg position during RALP may cause adverse events in patients (17,18), such as myocardial infarction and subsequent death (19), laryngeal edema (6), pulmonary edema (7), and optic ischemic neuropathy (8). Laryngeal edema occurred under pneumoperitoneum and prolonged (4.5 h) 45° head-down position (6). The pulmonary edema was attributed to prolonged (4 h) pneumoperitoneum with concomitant high intraabdominal pressure of up to 20 mmHg to minimize bleeding (7). Intraocular pressure reached peak levels at the end of 25° head-down position with pneumoperitoneum of 15 mmHg, on average 13.3 mmHg higher than the preinduction value in the supine position at the end of the Trendelenburg position. Time and PetCO₂ were the only significant covariates and the best linear fit from this model analysis is: Intraocular pressure (mmHg) = 7.95 + 0.21 × PetCO₂ (mmHg) + 0.053 × Trendelenburg time (min) (20). Optic ischemic neuropathy occurred after prolonged operation with steep Trendelenburg position (8). Intraocular pressure increases may be related to the occurrence of ischemic optic neuropathy. It may be

important for the surgeon to include ocular-specific questions in the preoperative assessment of patients. Operation in the head-down position with pneumoperitoneum should be completed in as short a time as possible to reduce the risks of complications. A previous report indicated that gas embolisms occurred associated with transesophageal echocardiography in 17% of patients with 15 mmHg pneumoperitoneum and 30° head-down position (21). Serious air embolism should be considered in patients with low cardiac function during RALP.

This study had some limitations. There were no significant differences in patient backgrounds between the groups, and this was a randomized control study, but the angle of the head-down position was changed from 20° to 30° in only one case after checking the operating field through a camera scope as it was difficult to change the angle after setting the robot. The operative field in this case was narrow because of the fat and bowel, therefore the decision to change the angle was made to obtain better operative field. The anesthesia conditions were not necessarily the same in each case as the anesthesiologist adjusted the anesthesia due to the patient's condition during the operation, but it was unavoidable to perform operation safely. The effects of pneumoperitoneum with head-down position in high-risk patients were not evaluated as only patients with low risk of cardiorespiratory function (ASA1-2) were included in this

study and actually no trouble was experienced in this study. The number of patients with high BMI was small in contrast to reports from western countries. Pneumoperitoneal pressure was 12 mmHg in this study, whereas some reports indicated that laparoscopic surgery could be performed safely with pneumoperitoneal pressure of 20 mmHg (22). Further research including not only different head-down position angle but also with different pneumoperitoneal pressures should be performed.

Conclusions

In the present study, we found that the pneumoperitoneum with head-down position in RALP influenced the cardiovascular and respiratory system to a greater extent than RRP, and these effects were stronger with deeper head-down angle. It is necessary to evaluate cardiovascular and respiratory function before RALP as the operation is considered to be safe in patients with ASA PS1-2. The operation should be finished in as short a time as possible to avoid complications. Shallow head-down angle may contribute to safety of RALP in high-risk patients with cardiovascular and respiratory system.

Conflict of interest

The authors have no conflict of interest to disclose.

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Figure legend

Fig.1

Each patient position placed in the 20° (A) and 30° (B) head-down during RALP

Fig. 2

Each mark demonstrates each measurement at each head-down setting and time point.

Correlations between head-down setting and MAP (A), PIP (B), and Cdyn (C) at each time point. T2, 5 min after Trendelenburg position with pneumoperitoneum; T3, 15 min after Trendelenburg position with pneumoperitoneum; T4, 30 min after Trendelenburg position with pneumoperitoneum; T5, 120 min after Trendelenburg position with pneumoperitoneum.

Table 1. Patient Characteristics and operative data

	RRP	RALP 20°	RALP 25°	RALP 30°
Total No. of patients	12	11	12	12
Age (years)	65.9±3.8	63.8±4.7	64.4±5.7	65.7±4.3
Body mass index (kg/m ²)	23.9±1.9	23.2±2.4	24.2±2.2	24.2±2.2
Anesthesia time (min)	333±33	300±31	317±27	303±30
Operating time (min)	248±30	212±27	218±32	218±44
Blood loss (mL)	1558±766	295±140*	295±156*	263±145*

Values are mean±SD or number

RRP, open radical retropubic prostatectomy; RALP, robot-assisted laparoscopic radical prostatectomy

*P<0.05 vs RRP

Table 2. Changes in hemodynamic and respiratory variables

	T0	T1	T2	T3	T4	T5	T6	T7
HR(bpm)								
RRP	60.2±5.0		57.8±5.2	57.3±5.0	56.9±5.2	58.3±5.4		61.1±5.6
RALP 20°	59.6±4.8	57.7±5.8	56.3±7.8	56.7±7.6	56.3±5.7	56.1±4.4	56.7±4.1	55.7±4.4
RALP 25°	59.9±8.9	59.3±7.2	59.0±8.4	59.0±9.1	58.5±8.8	59.9±9.9	60.4±7.0	59.4±7.0
RALP 30°	59.7±9.0	60.2±8.5	60.1±9.4	59.7±7.6	59.3±8.0	57.7±8.2	56.9±6.5	57.1±5.8
MAP(mmHg)								
RRP	72.6±8.7		70.9±8.4	68.3±7.4	68.1±7.7	72.5±7.2		71.5±7.4
RALP 20°	73.5±7.3	85.9±7.9#	87.6±8.9*#	83.9±9.8*	77.9±8.1	74.4±8.8	71.5±9.7	71.8±9.9
RALP 25°	72.5±8.3	86.5±5.8#	92.8±8.1*#	89.7±8.9*#	84.6±7.1*#	79.2±5.8	72.0±8.3	71.9±9.5
RALP 30°	73.0±9.8	86.8±8.6#	95.4±9.4*#	92.7±9.3*#	86.9±8.9*#	81.7±7.7	70.9±7.5	71.3±6.4
RR(breaths/min)								
RRP	10.4±1.3		10.0±1.1	10.3±1.1	10.4±1.3	10.8±1.4		10.7±0.9
RALP 20°	9.6±0.7	10.2±0.8	11.6±0.9*#	11.8±0.9*#	12.4±1.5*#	12.5±1.8*#	11.2±1.5	11.1±1.3
RALP 25°	9.7±1.4	10.4±1.9	12.1±2.5*#	12.5±2.5*#	12.7±2.4*#	13.1±2.8*#	11.7±1.8	11.4±1.9
RALP 30°	10.4±1.3	10.3±1.7	12.3±1.5*#	12.9±1.7*#	12.9±2.0*#	13.7±2.1*#	10.9±2.2	10.4±1.3
PetCO2(mmHg)								
RRP	32.8±2.8		32.7±2.5	32.4±2.7	32.8±2.9	32.9±2.2		32.8±2.1
RALP 20°	32.3±1.4	34.1±2.3	36.4±2.1*#	36.1±2.1*	36.2±3.3	36.7±3.5	34.9±3.0	33.9±3.0
RALP 25°	31.1±2.4	34.7±3.5	37.0±4.1*#	36.4±4.3*#	37.5±4.3*#	37.4±4.2*#	35.9±4.4	33.8±4.2
RALP 30°	31.3±3.2	34.3±3.0	37.6±4.9*#	38.2±5.6*#	37.6±5.0*#	37.6±5.0*#	33.7±4.4	32.6±3.7
PIP(cmH ₂ O)								
RRP	13.7±1.6		13.8±1.6	13.8±1.9	13.9±1.7	14.4±1.3		14.5±1.4
RALP 20°	14.0±1.6	20.2±2.7#	23.5±2.6*#	23.0±1.8*#	23.0±1.8*#	23.2±2.8*#	15.1±2.2	14.2±1.7
RALP 25°	14.5±1.8	21.0±2.5#	24.3±2.6*#	23.6±2.4*#	24.0±2.6*#	24.0±2.6*#	17.3±3.0	15.4±2.1
RALP 30°	14.9±2.1	20.9±2.5#	25.4±2.0*#	25.3±2.6*#	25.7±2.1*#	25.4±2.2*#	16.7±1.9	15.4±2.0
Cdyn(mL/cmH ₂ O)								
RRP	40.5±5.3		38.4±5.5	38.0±4.6	37.3±4.6	37.1±4.5		37.6±4.9
RALP 20°	38.9±5.1	27.0±4.1#	23.1±2.8*#	23.3±3.3*#	23.4±3.4*#	23.4±2.8*#	38.6±4.5	40.9±6.0
RALP 25°	40.3±5.8	25.9±6.0#	21.6±3.7*#	22.9±4.7*#	22.6±5.3*#	22.7±5.7*#	40.1±7.4	42.7±8.5
RALP 30°	37.8±4.3	25.6±4.8#	18.3±3.4*#	19.9±4.2*#	19.8±3.8*#	19.6±2.5*#	41.3±6.6	42.5±7.2

Values are mean±SD

*P<0.05 vs RRP in each time

¶P<0.05 vs RALP20° in T2

#P<0.05 vs T0 in each group

\$P<0.05 vs T1 in each group

T0, base line, immediately after anesthesia induction

T1, 5 minutes after pneumoperitoneum in supine position

T2, 5 minutes after Trendelenburg position with pneumoperitoneum in RALPs and 5 minutes after starting operation in RRP

T3, 15 minutes after Trendelenburg position with pneumoperitoneum in RALPs and 15 minutes after starting operation in RRP

T4, 30 minutes after Trendelenburg position with pneumoperitoneum in RALPs and 30 minutes after starting operation in RRP

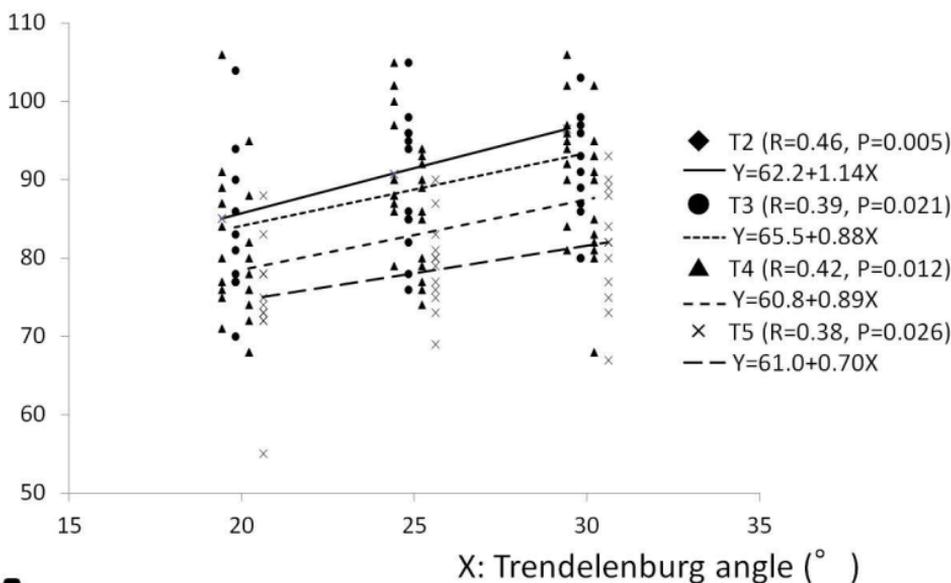
T5, 120 minutes after Trendelenburg position with pneumoperitoneum in RALPs and 120 minutes after starting operation in RRP

T6, 5 minutes after desufflation in supine position

T7, at skin closure in supine position

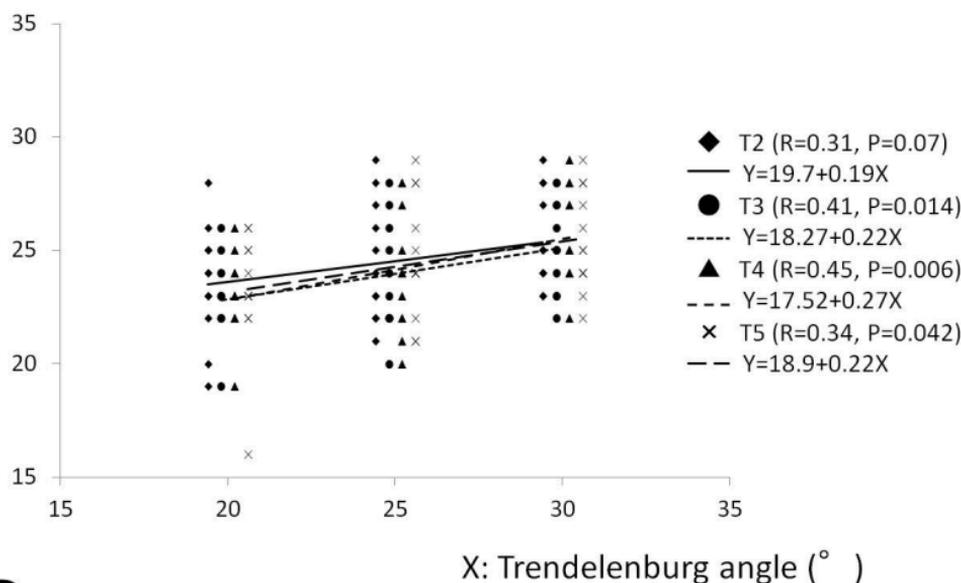


Y: MAP (mmHg)



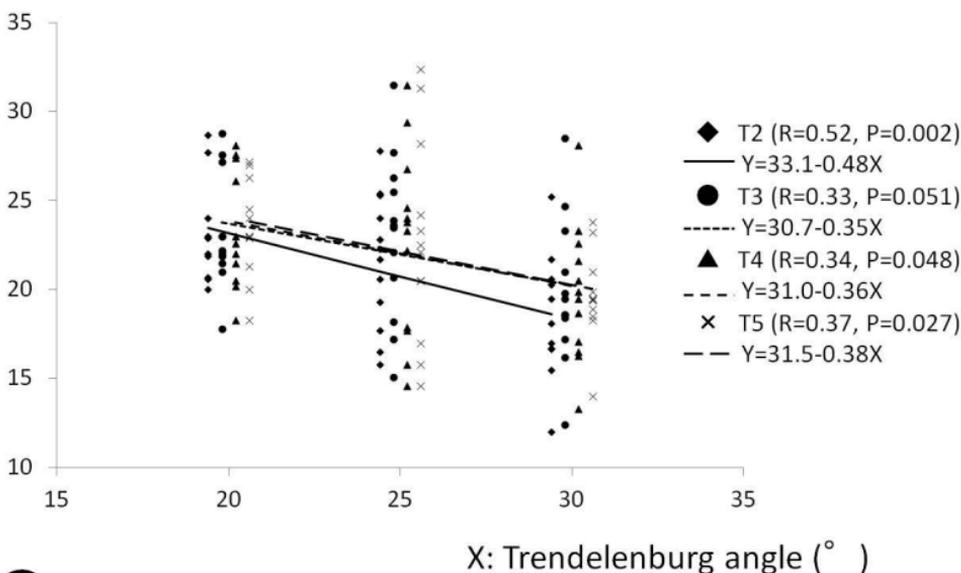
A

Y: PIP (mmHg)



B

Y: Cdyn (mL/cmH2O)



C